

## Evaluation of "Solitary" Thyroid Nodules in a Community Practice: A Managed Care Approach

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### **Abstract**

Evaluation of thyroid nodules remains a challenge for primary care physicians. To include or exclude the presence of malignancy in a thyroid nodule, radioisotope scan, ultrasound, and fine-needle aspiration biopsy of the thyroid generally are used. The objectives of this study were to determine the utility and cost effectiveness of fine-needle aspiration biopsy of solitary thyroid nodules in a community setting; to compare the cost of fine-needle aspiration biopsy with that of radioisotope scan and ultrasound; and to determine whether the practice of obtaining radioisotope scans and ultrasound has changed in the 1990s compared with the 1980s. Patients were referred by community physicians to university-based endocrinologists for evaluation of thyroid nodules. Many of the patients had previously undergone radioisotope scans and ultrasound scans at the discretion of their primary care physicians. All patients underwent fine-needle aspiration biopsy. The biopsy results were evaluated prospectively, and the practice of community physicians' obtaining radioisotope scans and ultrasound scans was compared for the 1980s and 1990s. Eighty-three patients underwent 104 biopsies. In 20 biopsies the specimens were inadequate; the others showed 70 benign, 9 suspicious, and 4 malignant lesions. All four patients with biopsy findings read as malignant were found to have malignant growth at surgical procedures. Two benign biopsy findings were false-negative results. Malignant growth was correctly diagnosed later for one patient at a second biopsy and for the other because of growth of the nodule. The cost of 104 biopsies was \$20,800. The cost of

radioisotope scans was \$22,400, and the cost of ultrasound scans was \$10,640. The frequency of obtaining radioisotope scans (84.5% vs 77%) and ultrasound scans (65% vs 45%) was slightly higher in the 1990s compared with the 1980s. Fine-needle aspiration biopsy is a safe and cost effective initial evaluation modality for smaller community-based centers, as it is at large tertiary centers. The cost incurred (\$33,040) in obtaining the radioisotope scans and ultrasound scans could have been saved if fine-needle aspiration biopsy had been used as the initial diagnostic procedure for evaluation of these nodules. Although radioisotope scan and ultrasound scan are of little diagnostic help in the evaluation of thyroid nodules, they continued to be obtained at a high frequency during the last decade.

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The management of thyroid nodules continues to be a frequent and challenging problem for family physicians, internists, and surgeons. The prevalence of thyroid nodules depends on the population studied and the method used for detection. In Framingham, MA, the prevalence of single, non-toxic thyroid nodules detected at physical examination of approximately 5000 persons was 3%.<sup>1</sup> On the other hand, in a routine autopsy study of patients with clinically normal thyroids, Mortensen et al<sup>2</sup> found a 49.5% prevalence of thyroid nodule. The prevalence of thyroid nodules among children has been reported to vary from 0.22%<sup>3</sup> to 1.5%.<sup>4</sup> In a study by Tunbridge et al,<sup>5</sup> the prevalence of thyroid nodules increased from 2% in the second decade of life to 5% in the seventh decade. These data indicate that the prevalence of thyroid nodularity increases with age.

The challenge in management of thyroid nodules is recognition of nodules that harbor malignant growth. The task is not easy because although thyroid nodules are frequent, thyroid cancer is very rare. Only about 25

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cases are diagnosed per million population per year.<sup>6</sup> Radioisotope scans, ultrasound scans, treatment with thyroid suppression, and fine-needle aspiration biopsy (FNAB) of the nodule have been used to improve the accuracy of estimation of the probability of malignant growth in a given thyroid nodule.<sup>7-9</sup>

In 1981, Ashcraft and Van Herle,<sup>7</sup> after a review of literature, concluded that FNAB should be the initial diagnostic test to evaluate a thyroid nodule. Since that time, the endocrinology section at Michigan State University has adopted this approach. However, it has also been suggested that to become proficient, an average physician needs to perform 100 to 200 aspirations in a short period. To maintain the skill of thyroid aspiration biopsy at a high level, about ten aspirations per week are required.<sup>9</sup> Because such large numbers are possible only in very large referral centers, it is implied that thyroid aspiration biopsies may not be efficient in smaller community hospital settings. Although we have adopted FNAB as the initial step in the evaluation of a thyroid nodule, many primary care physicians who practice in our area continue to use thyroid scintiscans or ultrasound scans or both of the thyroid according to their own clinical judgment. It is estimated that a large proportion of the patients who undergo these examinations are referred to our section for final disposition, because the only practicing endocrinologists in our community are located at the university. In recent years, additional reviews have appeared that recommend FNAB as the initial procedure in the management of thyroid nodules.<sup>10,11</sup> We therefore evaluated the clinical usefulness of these diagnostic procedures in our community-based setting. We attempted to estimate the cost of these procedures. In addition, we sought to determine whether the frequency of use of ancillary procedures (ultrasound and radioisotope scans) by the practicing physicians in our area had changed from the 1980s to the present (1995-1996).

#### ... METHODS ...

A total of 83 patients (70 women, 13 men) underwent thyroid aspiration at the Michigan State University Clinical Center from November 1981 through October 1989. The ages of the patients ranged from 16 to 71 years with a mean age of 40.2 years. All patients had a single palpable nodule. All biopsies were performed by two staff endocrinologists or by an endocrinology fellow under supervision. A 25-gauge needle was inserted into the nodule without anesthesia with the aid of a syringe fitted into a special holder. Smears were made from the aspirates on glass slides and were fixed in alcohol or air dried. The slides were

stained with Giemsa stain or by means of Papanicolaou method. The smears were interpreted by pathologists at two area hospitals, and the findings were classified as inadequate for diagnosis, benign lesion, suggestive of malignant growth, or malignant lesion. A specimen was considered inadequate for diagnosis if it appeared acellular or bloody, had poor fixation, or contained only histiocytes, inflammatory cells, lymphocytes, or colloid. If an inadequate specimen was obtained, biopsy was repeated until a satisfactory specimen was obtained.

Benign specimens contained cellular architecture consistent with nodular goiter, lymphocytic thyroiditis, or granulomatous thyroiditis. A specimen was considered suggestive of malignant growth if it contained papillary clusters or follicular cells, hypercellularity, atypical follicular cells, Hürthle cells without evidence of lymphocytic thyroiditis, clear nuclear inclusions, or psammoma bodies. Malignant specimens demonstrated architecture consistent with the corresponding type of malignant tumor.

All radioisotope scans and ultrasound studies were requested by primary care physicians. Radioactive scintiscans were obtained at area hospitals with either iodine 123 or technetium 99m. Ultrasound scans also were obtained at the area hospitals. A review of the charts of 45 patients referred for evaluation of "thyroid nodule" during 1995-1996 was conducted to determine whether the practice of ordering thyroid ultrasound and radioisotope scans had changed in the 1990s compared with 1980s.

#### ... RESULTS ...

Eighty-three patients underwent 104 FNABs. Twenty of the specimens were considered inadequate or insufficient. Fifteen patients required two and three patients required three aspirations, but eventually all patients had a biopsy specimen that could be evaluated. All patients tolerated the procedure well except for minor discomfort at the time of the procedure; no other complications were observed. Seventy biopsy results were considered benign. Nine had findings suggestive of malignancy and four were considered malignant (Table 1). One patient underwent a second biopsy after the initial biopsy specimen was read as benign, and the second biopsy had findings suggestive of malignancy. Nineteen patients underwent surgical procedures, and nine of these had malignant lesions. Four lesions were diagnosed as Hürthle cell tumors, four as papillary carcinomas, and one as follicular carcinoma.

Eleven patients with benign cytologic findings at the initial biopsy underwent thyroidectomy for cosmetic or personal reasons; nine of the lesions were benign. One patient had continued growth of the nodule at the first follow-up visit after the first benign biopsy result and underwent a second biopsy, the findings of which was suggestive of malignant growth. One patient had continued slow growth over a 4-year follow-up period and underwent an operation without undergoing a second biopsy. Both of these patients were found at operation to have a malignant lesion. The other patients have undergone follow-up examinations either at the Michigan State University endocrinology clinic or with their private physicians (we obtained follow-up data from them) and have not had any clinical evidence of malignant disease. The mean follow-up period for these patients was 24.5 months. Although malignant tumors of the thyroid may be slow growing, it appears that 2 of 70 (3%) biopsies had false-negative findings of malignancy.

Nine patients with suggestive cytologic findings were advised to undergo surgical treatment, but only four did so. Three of these patients were found to have thyroid carcinoma, and one was found to have follicular adenoma. Five patients who did not undergo surgical treatment underwent follow-up examinations for a mean of 23.6 months and did not show any clinical evidence of malignant disease.

All four patients with malignant cytologic findings underwent operations and were found to have malignant lesions. Three of these lesions were Hürthle cell tumor, and one was papillary carcinoma.

The average cost of FNAB, including interpretation by the pathologist in our area, was approximately \$200. Because the actual cost of these procedures could not be obtained, these figures represent the average charge in 1997. Thus the total cost for all biopsies in this study was \$20,800.

Sixty-four patients underwent radioisotope scans and 38 underwent ultrasound scans. Thirty-three patients underwent both types of examination. The findings on the radioisotope scans are shown in Table 2. Nearly 90% of the patients referred for additional evaluation had "cold" nodules. (Cold nodules are areas of decreased radioactivity.) The average cost of radioisotope scans in our area, including interpretation by a radiologist, is approximately \$350. The total cost for all the radioisotope scans in this study was approximately \$22,400.

The findings at ultrasound examination are shown in Table 3. Only four patients (10.5%) were found to have pure cysts; the other lesions found were either solid or mixed. The average cost of ultrasound scans, including interpretation by a radiologist in our area, is approximately \$280. The total cost for 38 ultrasound scans was approximately \$10,640.

We reviewed the charts of the last 45 patients referred to us for evaluation of thyroid nodules in

**Table 1.** Results of Fine-Needle Aspiration Biopsy (n = 84)

Biopsy Finding	Treatment	Correct Diagnosis
70 Benign*	11 Operated on	2 Malignant*
	59 Followed up	9 Benign Appear benign
9 Suspicious	4 Operated on	3 Malignant 1 Benign
	5 Followed up	Appear benign
4 Malignant	4 Operated on	4 Malignant

\*One patient with benign findings underwent a second biopsy, the findings of which were suggestive of malignant growth.

**Table 2.** Results of Radioisotope Scans (n = 64)

Type	No. of Patients	Percentage
Cold	56	87.5
Patchy	3	4.6
Hot or Warm	3	4.6
Multinodular	1	1.5
Normal	1	1.5

**Table 3.** Results of Ultrasound Examination (n = 38)

Type	No. of Patients	Percentage
Cystic	4	10.5
Solid	12	31.5
Mixed	20	52.6
Normal	2	5.2

1995–1996. Thirty-eight patients (84%) already had undergone nuclear medicine scans when referred; 29 patients (64%) had already undergone ultrasound scans of the thyroid. In seven instances, after the radioisotope scan was obtained, an ultrasound scan was recommended by the radiologist. In one additional instance, the ultrasound scan was performed immediately after the radioisotope scan before the patient left the radiology facility. That is, 8 of 45 (17.5%) ultrasound scans were initiated by the radiologist. In two instances, radioisotope scans were not obtained because the patients were pregnant. In one instance a radioisotope scan was suggested by the radiologist after the ultrasound scan was obtained.

... DISCUSSION ...

The challenge in the management of thyroid masses in the neck is to differentiate benign from malignant lesions. For this purpose, a radioactive scan (iodine or technetium) and ultrasound examination of the mass and FNAB are performed. In this study, we confirmed that FNAB is safe and effective in a community setting. (Michigan State University College of Human Medicine is a community-based medical school. At the time of this study, the only two endocrinologists practicing in the community were based at the medical school.) Moreover, we found that the routine use of ultrasound and radioisotope scans as the initial step in the evaluation of thyroid masses is not very cost effective.

Virtually all thyroid diseases can present as a mass in the neck. According to Molitch et al<sup>12</sup> the mean probability of carcinoma in a distinct nodular thyroid mass is 10.9%. Given the sensitivity and specificity of radioisotope scans and ultrasound scans and the probabilities of carcinoma, one can calculate the likelihood that an abnormal radioisotope scan or ultrasound scan would suggest carcinoma. The data of Van Herle et al<sup>9</sup> were used in the calculation. If the ultrasound scan is per-

formed first, the probability of finding carcinoma in a nodule rises from 10.9% to only 13% if the ultrasound scan is abnormal (solid or mixed). The probability falls to 2.0% if a pure cyst is found. A radioisotope scan performed first and showing a cold nodule raises the baseline probability of the presence of carcinoma from 10.9% to 16.9%. Obtaining both studies for a patient improves only slightly the estimated probability of detecting malignant growth. The probability of carcinoma in a hot nodule (an area of increased radioactivity) on a radioisotope scan is extremely low, but there are not sufficient data to calculate the probability of the presence of malignant growth in hot nodules, because most of the patients do not undergo operations.

Our results show that 77% (64/83) of our patients underwent radioisotope scans and 46% (38/83) underwent ultrasound scans. Of these, 40% (33/83) underwent both radioisotope scans and ultrasound scans. Although decision-analysis considerations and articles in the literature suggest that ultrasound and radioisotope scans are diagnostically not very helpful, these diagnostic studies were frequently ordered in both the 1981 through 1989 study and the 1995–1996 survey. As a matter of fact, the frequency of radioisotope scans and ultrasound scans ordered by primary care physicians was slightly higher in the 1995–1996 survey compared with the 1981–1989 period (Table 4). From the results of this study, we are not able to determine how many patients were not referred for FNAB by primary care physicians because of a pure cyst on an ultrasound scan or a hot nodule on a radioisotope scan. However, it appears from the results for patients who were referred that according to findings on ultrasound scans and radioisotope scan, nearly 90% of patients required needed FNAB (90% of lesions were mixed on ultrasound scans, and nearly 90% of lesions were cold on radioisotope scans). Not obtaining these studies could have saved the money spent on radioisotope scans and ultrasound scans (approximately \$33,040).

In our community, ultrasound scans are frequently suggested by radiologists. In a separate study, we observed<sup>13</sup> that after a radioisotope scan was performed, in 57% of instances it was suggested by the radiologist that an ultrasound scan be obtained. In 83% of such instances, an ultrasound scan was performed without the knowledge of the referring physician. In the 1995–1996 survey, however, radiologists suggested ultrasound scans in fewer instances (17.5%).

**Table 4.** Frequency of Radioisotope Scans and Ultrasound Scans Requested by Primary Care Physicians in the Evaluation of Thyroid Nodules

Time Period; n	Radioisotope Scan (%)	Ultrasound Scans (%)	Both
1981–1989 (83)	64 (77)	38 (46)	33 (40)
1995–1996 (45)	38 (84)	29 (64)	26 (58)

It appears that the main reason physicians obtain an ultrasound scan is the incorrect assumption that pure cystic lesions are frequent and that the procedure will be helpful to exclude or make a correct diagnosis of carcinoma. In our study, only 10.5% of lesions were found to be pure cysts, whereas other authors have reported a frequency of pure cysts ranging from 1 of 550<sup>14</sup> to 17%.<sup>15</sup> Physicians also appear to believe that two studies are better than one. The results of the Bayesian analysis discussed earlier shows that an ultrasound scan adds little diagnostic information.

The literature offers many opinions for and against ultrasound imaging.<sup>16-20</sup> Most articles seem to suggest that ultrasound offers little help for or against the diagnosis of carcinoma in a thyroid nodule. We agree strongly. It appears that obtaining thyroid ultrasound scans in the evaluation of solitary thyroid nodules has little added utility, and it increases cost. However, in spite of these considerations, our 1995-1996 review showed little change in requests for ultrasound scans by primary care physicians.

Radioisotope scans also are of limited utility. It is generally believed that if the presence of a cold palpated nodule increases the likelihood of the presence of malignant growth in that nodule,<sup>21</sup> whereas hyperfunctioning nodules are almost always benign.<sup>7</sup> As early as 1964, Katsutaro and Sokal<sup>21</sup> commented "it would appear that, although scintiscan is a useful aid in the study of patients with thyroid disease and may occasionally be helpful in excluding thyroid cancer, it cannot be expected to solve the problem of differentiating between benign and malignant goiters." We believe that this statement is true today. We believe that the preferred approach to a thyroid nodule is to first obtain an FNAB. If the biopsy results are equivocal, another biopsy should be performed. If the second biopsy does not yield diagnostic information, management strategy should be based on the overall clinical assessment. Radioisotope scans may be helpful in selected instances in that a cold nodule may have to be excised under these circumstances. This approach is in agreement with approaches suggested by many others.<sup>10,11,22</sup>

Compared with the results of other published reports, our results of FNAB are remarkably similar. In a review based on pooled results for 18,183 patients from seven series, it was observed that 69% of biopsies had benign findings (ours 67.3%), 10% were suspicious (ours 8.6%), 4% were malignant (ours 3.8%), and 17% were nondiagnostic (ours 19.2%).<sup>22</sup> Although the true sensitivity and specificity of FNAB cannot be calculated (because all patients were not operated on by us or others), the apparent sensitivity and specificity

in our series are similar to those in larger published series.<sup>22</sup> Although some authors have reported a higher rate of inadequate smears for community-based clinicians,<sup>23</sup> our rate for unsatisfactory smears was similar to those in larger series.<sup>22</sup>

We concluded that FNAB of the thyroid is an effective initial diagnostic test for maximizing the number of malignant tumors found at operation and minimizing the number of operations for benign lesions. It can be used in a community teaching hospital with the same degree of accuracy as in tertiary referral centers. Substantial savings can be realized with this approach. Results similar to ours have been reported by others in a rural practice setting<sup>24</sup> and in an average-size healthcare facility.<sup>25</sup> These studies also indicate that performing a large number of thyroid aspirations per week may not be required to maintain competency in this procedure, as has been suggested by some authors.<sup>9</sup> However, the minimum number of thyroid aspirations needed to become proficient and maintain competency remains to be established. The results of our study also suggested that for the cost-effective management of thyroid masses, procedures have to be developed to alert physicians that the ancillary diagnostic procedures (radioisotope scans and ultrasound scans) are of little value in changing diagnostic likelihoods and only add to the cost of care of these patients.

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